Complete Summary

GUIDELINE TITLE

Management of fibromyalgia syndrome.

BIBLIOGRAPHIC SOURCE(S)

Goldenberg DL, Burckhardt C, Crofford L. Management of fibromyalgia syndrome. JAMA 2004 Nov 17;292(19):2388-95. [118 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

On October 17, 2005, Eli Lilly and the U.S. Food and Drug Administration (FDA) notified healthcare professionals of revision to the PRECAUTIONS/Hepatotoxicity section of the prescribing information for Cymbalta (duloxetine hydrochloride), indicated for treatment of major depressive disorder and diabetic peripheral neuropathic pain. Postmarketing reports of hepatic injury (including hepatitis and cholestatic jaundice) suggest that patients with preexisting liver disease who take duloxetine may have an increased risk for further liver damage. The new labeling extends the Precaution against using Cymbalta in patients with substantial alcohol use to include those patients with chronic liver disease. It is recommended that Cymbalta not be administered to patients with any hepatic insufficiency. See the FDA Web site for more information.

COMPLETE SUMMARY CONTENT

IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Fibromyalgia syndrome

GUIDELINE CATEGORY

Management
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Neurology
Nursing
Pharmacology
Physical Medicine and Rehabilitation
Psychiatry
Psychology
Rheumatology

INTENDED USERS

Advanced Practice Nurses
Nurses
Pharmacists
Physical Therapists
Physician Assistants
Physicians
Psychologists/Non-physician Behavioral Health Clinicians

GUIDELINE OBJECTIVE(S)

To provide up-to-date evidence-based guidelines for the optimal treatment of fibromyalgia syndrome (FMS)

TARGET POPULATION

Patients suffering from fibromyalgia syndrome

INTERVENTIONS AND PRACTICES CONSIDERED

1. Fibromyalgia syndrome diagnosis confirmation
2. Pharmacological treatment including:
    - Amitriptyline and cyclobenzaprine

- Tramadol with or without acetaminophen
- Serotonin reuptake inhibitors (SSRIs), such as fluoxetine
- Serotonin and epinephrine reuptake inhibitors (SNRIs), such as venlafaxine, milnacipran, duloxetine
- Pregabalin
- Guideline developers considered but did not recommend the following pharmacological therapies with weak evidence for efficacy: Growth hormone, 5-hydroxytryptamine (serotonin), tropisetron, and S-adenosyl-methionine.
- Guideline developers considered but did not recommend the following pharmacological therapies with no evidence for efficacy: opioids, corticosteroids, nonsteroidal anti-inflammatory drugs, benzodiazepine and nonbenzodiazepine hypnotics, melatonin, calcitonin, thyroid hormone, guaifenesin, dehydroepiandrosterone, magnesium

3. Non-pharmacological therapies including:
    - Cardiovascular exercise
    - Cognitive behavioral therapy
    - Patient education, using lectures, written materials, demonstrations
    - Multidisciplinary therapy, such as exercise and cognitive behavioral therapy, or education and exercise
    - Strength training, acupuncture, hypnotherapy, biofeedback, balneotherapy
    - Guideline developers considered but did not recommend the following non-pharmacological therapies with weak evidence for efficacy: Chiropractic, manual and massage therapy, electrotherapy, ultrasound.
    - Guideline developers considered but did not recommend the following non-pharmacological therapies with no evidence of efficacy: Tender (trigger) point injections, flexibility exercise
4. Specialist referral

MAJOR OUTCOMES CONSIDERED

Effect of treatment on visual analog pain scores, pain threshold, psychological function (depression, anxiety), quality of life, fatigue, sleep, and 6-minute walk

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

A search of all human trials (randomized controlled trials and meta-analyses of randomized controlled trials) of FMS was made using Cochrane Collaboration Reviews (1993-2004), MEDLINE (1966-2004), CINAHL (1982-2004), EMBASE (1988-2004), PubMed (1966-2004), Healthstar (1975-2000), Current Contents (2000-2004), Web of Science (1980-2004), PsychInfo (1887-2004), and Science Citation Indexes (1996-2004). The literature review was performed by an interdisciplinary panel, composed of 13 experts in various pain management

disciplines, selected by the American Pain Society (APS), and supplemented by selected literature reviews by APS staff members and the Utah Drug Information Service. References were consistently checked electronically for any relevant articles.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Strength of Evidence

Strong - positive results from a meta-analysis or consistently positive results from more than 1 randomized controlled trial (RCT)

Moderate - positive results from 1 RCT or largely positive results from multiple RCTs or consistently positive results from multiple non-RCT studies

Weak - positive results from descriptive and case studies, inconsistent results from RCTs, or both

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Strength of evidence (strong, moderate, weak) definitions are repeated at the end of "Major Recommendations" field.

There is strong evidence to support the use of low-dose tricyclic medications, such as amitriptyline and cyclobenzaprine, as well as cardiovascular exercise, cognitive behavioral therapy (CBT), patient education, or a combination of these for the management of fibromyalgia syndrome (FMS). There is moderate evidence that tramadol, selective serotonin reuptake inhibitors (SSRIs), serotonin and epinephrine reuptake inhibitors (SNRIs), and certain anticonvulsants are effective but the complete results of some trials are not available and systematic reviews have not been reported. Moderate evidence exists for the efficacy of strength training exercise, acupuncture, hypnotherapy, biofeedback, massage, and warm water baths. Many of the commonly used FMS therapies have not been carefully evaluated. Based on these reports, a stepwise FMS management guideline can be recommended.

Stepwise Fibromyalgia Management

Step 1

- Confirm the diagnosis.
- Explain the condition.
- Evaluate and treat comorbid illness, such as mood disturbances and primary sleep disturbances.

Step 2

- Trial with low-dose tricyclic antidepressant or cyclobenzaprine
- Begin cardiovascular fitness exercise program.
- Refer for cognitive behavior therapy or combine that with exercise.

Step 3

- Specialty referral (e.g., rheumatologist, physiatrist, psychiatrist, pain management)

- Trials with selective serotonin reuptakes inhibitors, serotonin and norepinephrine reuptake inhibitors, or tramadol
- Consider combination medication trial or anticonvulsant.

The FMS diagnosis first must be confirmed and the condition explained to the patient and family. Any comorbid illness, such as mood disturbances or primary sleep disturbances, should be identified and treated. Medications to consider initially are low doses of tricyclic antidepressants or cyclobenzaprine. Some SSRIs, SNRIs, or anticonvulsants may become first-line FMS medications as more RCTs are reported. All patients with FMS should begin a cardiovascular exercise program. Most patients will benefit from CBT or stress reduction with relaxation training.

A multidisciplinary approach combining each of these modalities may be the most beneficial. Other medications such as tramadol or combinations of medications should be considered. Patients with FMS not responding well to these steps should be referred to a rheumatologist, physiatrist, psychiatrist, or pain management specialist.

Treatment of Fibromyalgia Syndrome

Medications

Strong Evidence for Efficacy

- Amitriptyline: often helps sleep and overall well-being; dose, 25-50 mg at bedtime
- Cyclobenzaprine: similar response and adverse effects; dose, 10-30 mg at bedtime

Modest Evidence for Efficacy

- Tramadol: long-term efficacy and tolerability unknown; administered with or without acetaminophen; dose, 200-300 mg/d
- Serotonin reuptake inhibitors (SSRIs):
    - Fluoxetine (only one carefully evaluated at this time): dose, 20-80 mg; may be used with tricyclic given at bedtime; uncontrolled report of efficacy using sertraline.
- Dual-reuptake inhibitors (SNRIs):
    - Venlafaxine: 1 RCT ineffective but 2 case reports found higher dose effective
    - Milnacipran: effective in single randomized control trial (RCT)
    - Duloxetine: effective in single RCT
- Pregabalin: second-generation anticonvulsant; effective in single RCT

Weak Evidence for Efficacy

- Growth hormone: modest improvement in subset of patients with FMS with low growth hormone levels at baseline
- 5-Hydroxytryptamine (serotonin): methodological problems
- Tropisetron: not commercially available

- S-adenosyl-methionine: mixed results

No Evidence for Efficacy

- Opioids, corticosteroids, nonsteroidal anti-inflammatory drugs, benzodiazepine and nonbenzodiazepine hypnotics, melatonin, calcitonin, thyroid hormone, guaifenesin, dehydroepiandrosterone, magnesium.

Nonmedicinal Therapies

Strong Evidence for Efficacy (Wait-List or Flexibility Controls But Not Blinded Trials)

- Cardiovascular exercise: efficacy not maintained if exercise stops
- CBT: improvement often sustained for months
- Patient education: group format using lectures, written materials, demonstrations; improvement sustained for 3 to 12 months
- Multidisciplinary therapy, such as exercise and CBT or education and exercise.

Moderate Evidence for Efficacy

- Strength training, acupuncture, hypnotherapy, biofeedback, balneotherapy

Weak Evidence for Efficacy

- Chiropractic, manual, and massage therapy; electrotherapy, ultrasound

No Evidence for Efficacy

- Tender (trigger) point injections, flexibility exercise

Definitions

Strength of Evidence

Strong - positive results from a meta-analysis or consistently positive results from more than 1 randomized controlled trial (RCT)

Moderate - positive results from 1 RCT or largely positive results from multiple RCTs or consistently positive results from multiple non-RCT studies

Weak - positive results from descriptive and case studies, inconsistent results from RCTs, or both

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Improved management of fibromyalgia syndrome

POTENTIAL HARMS

Adverse effects of medications

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

There are major limitations to the fibromyalgia syndrome (FMS) literature, with many treatment trials compromised by short duration and lack of masking. There are no medical therapies that have been specifically approved by the US Food and Drug Administration for management of FMS. Nonetheless, current evidence suggests efficacy of low-dose tricyclic antidepressants, cardiovascular exercise, cognitive behavioral therapy, and patient education. A number of other commonly used FMS therapies, such as trigger point injections, have not been adequately evaluated.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Staff Training/Competency Material

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2004 Nov 17

GUIDELINE DEVELOPER(S)

American Pain Society Fibromyalgia Panel - Independent Expert Panel

SOURCE(S) OF FUNDING

American Pain Society

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Although this guideline was sponsored by the American Pain Society, the group did not participate in the design and conduct of the study, in the collection, analysis, and interpretation of the data, or in the preparation, review, or approval of the manuscript.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available to subscribers only from the Journal of the American Medical Association Web site.

Print copies: Available from Don L. Goldenberg, MD, Department of Rheumatology, Newton-Wellesley Hospital, 2000 Washington St, Newton, MA 02462 (dgoldenb@massmed.org)

AVAILABILITY OF COMPANION DOCUMENTS

A continuing medical education (CME) course on the management of fibromyalgia syndrome is available by subscription from the Journal of the American Medical Association Web site.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on March 23, 2005. The information was verified by the guideline developer on March 30, 2005. This summary was updated by ECRI on October 20, 2005, following the U.S. Food and Drug Administration advisory on Cymbalta (duloxetine hydrochloride).

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